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Peritoneal Dialysis Treatment Modality Option in Acute Kidney Injury

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Key Words
Peritoneal dialysis · Acute kidney injury

Abstract
Background: Peritoneal dialysis (PD) may be a feasible and safe alternative to haemodialysis not only in the chronic but also in the acute setting. It was previously widely accepted as a modality for acute kidney injury (AKI) treatment, but its practice declined in favor of other types of extracorporeal therapies. ***Summary:*** The interest in PD to manage AKI patients has been increased and PD is now frequently used in developing countries because of its lower cost and minimal infrastructural requirements. Studies from these countries have shown that, with careful thought and planning, critically ill patients can be successfully treated using PD. Some of the classic limitations of PD use in AKI, such as infectious and mechanical complications and poor metabolic control, have been decreased with the use of cyclers, flexible catheters, and a high volume of dialysate. The recent publication of the International Society of Peritoneal Dialysis guidelines for PD in AKI has tried to address these issues and provide an evidence-based standard by which to initiate therapy. ***Key Message:*** In this review, advances in technical aspects and the advantages and limitations of PD were discussed; it clearly showed that PD is a simple, safe, and efficient way to correct metabolic, electrolyte, acid – base, and volume disturbances generated by AKI and it can be used as a renal replacement therapy modality to treat AKI, both in and out of the intensive care unit setting.

Historical Aspects

The quantum of research about acute peritoneal dialysis (PD) considerably reduced with an increase in the uptake of more technologically attractive options such as haemofiltration (HF) and haemodialysis (HD). In the late 1990s and 2000s, several concerns were raised regarding acute PD; some of the issues were with regard to whether sufficient clearances and ultrafiltration could be achieved and regarding peritonitis risk and the effects of protein loss and glucose absorption. All of these reasons led to relegating PD to be used only in countries where resources would not allow the use of the more 'advanced therapies', and hence, PD is predominantly practiced only in the developing world.

Gaiao et al. [1] performed a survey among delegates at three major dialysis congresses and found that 36% felt PD was suitable for acute kidney injury (AKI) in the intensive care unit (ICU); however, only 15% actually practiced it. In the same study, it was observed that PD was far more likely to be practiced by physicians from Asia compared to those from Europe and North America. Over the past decade, there has been resurgence in the use of PD for AKI. This has largely been triggered by a Brazilian group whose research has shown PD to be a safe treatment option with outcomes comparable to HD. PD has also been chosen as the modality of choice for treating AKI by the International Society of Nephrology 0by25 initiative and this is largely being driven through the Saving Young Lives Campaign where centres in develop-

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Table 1. Advantages and disadvantages of PD in AKI

Advantages	Disadvantages
Technically simple	Requires intact peritoneal cavity with adequate membrane function
No need for expensive equipment	It may not be adequate for severe acute pulmonary edema or life-threatening hyperkalemia
It avoids vascular access	Infection (peritonitis) can occur
It ensures minimum blood loss	Ultrafiltration and clearance cannot be exactly predicted
Biocompatible	It can cause protein losses
Useful in all types of AKI	It can cause hyperglycaemia and hypernatraemia
More rapid renal recovery	It may impair respiratory mechanics
It provides continuous RRT and cardiovascular stability	Lactate buffer
Beneficial in select patients population (children, heart failure, cirrhosis, bleeding diathesis).	

ing countries in Africa and Asia are supported in setting up acute PD programs for the treatment of AKI.

PD has a number of advantages over other therapies (table 1). It has been well demonstrated that acute PD requires less infrastructure than extracorporeal therapies and is more cost effective. Two studies from India showed that acute PD costs approximately half the cost for HD or continuous HF and Kilonzo et al. [2] showed that it costs approximately $350 for every life saved when using manual acute PD with 2 hourly exchanges.

PD may be a better option for patients with difficult vascular access especially in the pediatric population. Solute removal is gradual with less potential for disequilibrium syndrome and intracranial fluid shifts, making it a modality option among patients with increased intracranial pressure [3].

Since no extracorporeal circulation is required, there is relatively good hemodynamic tolerance, and local renal hemodynamics may be better preserved. It has also been postulated that PD may be more physiologic and less inflammatory than extracorporeal therapies, which involve the exposure of blood to synthetic membranes. These factors when combined could potentially contribute to the earlier recovery of renal function as reported by some other studies [4–7].

The increase in PD penetration in the area of AKI and the significant variability of practice patterns published in the literature led the International Society of Peritoneal Dialysis (ISPD) to develop guidelines for the method of performing acute PD in AKI in order to guide practitioners, many of whom were non-nephrologists [4]. The guidelines recommend that PD is a suitable modality for treatment of AKI, giving confidence to practitioners that treating AKI with PD in this scenario is a safe and effective practice. The rationale for this recommendation and practical aspects of PD for AKI are presented below.

PD Adequacy in AKI

With increasing interest being shown in using PD to manage patients with AKI [3, 8–16], the first question that must be asked is whether PD can provide adequate clearance in the treatment of these patients [6, 12, 13].

A study focusing on acute PD in the setting of hypercatabolic AKI using rigid catheters and either continuous equilibrated PD (CEPD) or tidal PD using a cycler, showed that CEPD with 4 hourly exchanges achieved a weekly Kt/V of 1.8 and for tidal APD, it was 2.34 [14].

An initial Brazilian pilot study assessed the efficacy of high volume (HV) PD in a prospective study of 30 consecutive AKI patients [15]. PD was performed using a Tenckhoff catheter, 2 litres exchanges, and 35–50 min dwell times. The prescribed Kt/V value was 0.65 per session, the duration of each session was 24 h, and a total dialysate volume of 36–44 litres/day. HVPD was rapidly effective in the correction of BUN, creatinine, bicarbonate, and fluid overload. The achieved weekly Kt/V was 3.8 ± 0.6 and the mortality was 57%. Five years later, they published another prospective study on 204 patients.

AKI patients were treated with HVPD (prescribed Kt/V = 0.60/session) [16]. BUN and creatinine levels stabilized after 4 sessions to around 50 and 4 mg/dl, respectively. Weekly delivered Kt/V was 3.5 ± 0.68 and the mortality rate was 57.3%. Old age and sepsis were identified as risk factors for death. Persistence of urine output, increases of 1 g in nitrogen balance (NB) and achieving >500 ml in UF after 3 sessions were identified as favorable prognostic factors. It was concluded that HVPD is effective in selected patients; however, if after 3 sessions, UF is low or NB is negative, substitution or addition of HD should be considered.

These studies from Botucatu, Sao Paulo, Brazil, demonstrated that using cycler therapy, flexible catheters and HVs of fluid, critically ill AKI patients can be successfully treated with PD and that both adequate small solute clearances and ultrafiltration can be achieved [3, 15, 16].

Solute clearance in PD is limited by dialysate flow, membrane permeability and surface area in contact with dialysate (KoA) [3, 9, 16]. Exchanges of 2 litres lasting approximately 1 h can achieve a saturation of the spent dialysate in the range of 50%. This means that, over 24 h, a daily Kt/V of 0.5 in a patient with body weight between 60 and 65 kg can be achieved [3, 7, 16].

Ponce et al. [17], performed a trial to assess dosing patterns of PD in critically ill AKI patients, randomized to receive higher or lower intensity PD therapy (prescribed weekly Kt/V of 5.6 vs. 3.5). The 2 groups had similar mortality rates after 30 days (55 vs. 53%, p = 0.83). This trial concluded that increasing the intensity of HVPD does not reduce mortality and does not improve metabolic control. Weekly delivered Kt/V of 3 is sufficient to maintain adequate metabolic control in AKI patients, with no difference in survival compared to patients who received a weekly Kt/V of 4.2.

According to the ISPD guideline, PD for AKI recommendations, where resources permit, targeting a weekly Kt/V urea of 3.5 provides outcomes comparable to those of daily HD; targeting higher doses does not improve outcomes. This dose may not be necessary for many AKI patients and targeting a weekly Kt/V of 2.1 may be acceptable; however, to date there is no evidence to prove this [4] (fig. 1).

PD Outcomes in AKI

The next question is whether PD is comparable to other dialysis methods in AKI patients. The answer to that question is neither simple nor easy to find under prevailing conditions. The various modalities of acute renal replacement therapy (RRT) present advantages and disadvantages under specific circumstances; the spectrum of therapies for AKI should therefore be considered more a continuum than a series of modalities to be compared, one to the other.

Few studies have compared PD with other dialysis methods in AKI patients, and reports present conflicting information with regard to efficacy and cost. Phu et al. [18] compared intermittent PD with continuous RRT, and they demonstrated a worse outcome in patients treated with PD. This study was stopped early due to a higher mortality in the PD arm. In addition to criticisms about the PD method and the high peritonitis rate, this study of acutely ill patients with sepsis or malaria showed that with continuous RRT the mortality was only 15%, which is far lower than the mortality observed in most ICU settings offering continuous RRT.

George et al. [19] performed a randomized study to compare continuous RRT and continuous PD in critically ill patients. No difference was observed with regard to the correction of metabolic parameters and fluid overload. Urea and creatinine clearances were higher and fluid correction was faster with continuous RRT. The mortality rates in the 2 study groups were similar. Unfortunately, the study was underpowered and performed using both peritoneal and continuous RRT clearances below which the values were considered optimal. Along with rigid catheters, locally available PD fluids and manual exchanges were used.

A randomized study performed in Brazil with 120 AKI patients compared HVPD versus daily intermittent HD [3]. Baseline characteristics were similar in both groups, which included old patients, high APACHE II scores, and vasoactive drugs use (>60%). Both RRT modalities achieved metabolic and acid – base control. Mortality did not differ significantly between the 2 groups (58 vs. 53%, p = 0.48). The rate of renal recovery was similar for both modalities, but HVPD was associated with a significantly shorter time to recovery (7.2 ± 2.6 vs. 10.6 ± 4.7 days).

The same Brazilian group performed another prospective study comparing the effect of HVPD and prolonged HD (PHD) on AKI patients' outcome [20]. Delivered Kt/V and ultrafiltration were higher in the PHD group; however, there was no difference between the 2 groups in mortality and recovery of kidney function or need for chronic dialysis.

Al-Hweish [21] in Saudi Arabia recently presented a randomized controlled trial of tidal PD compared with

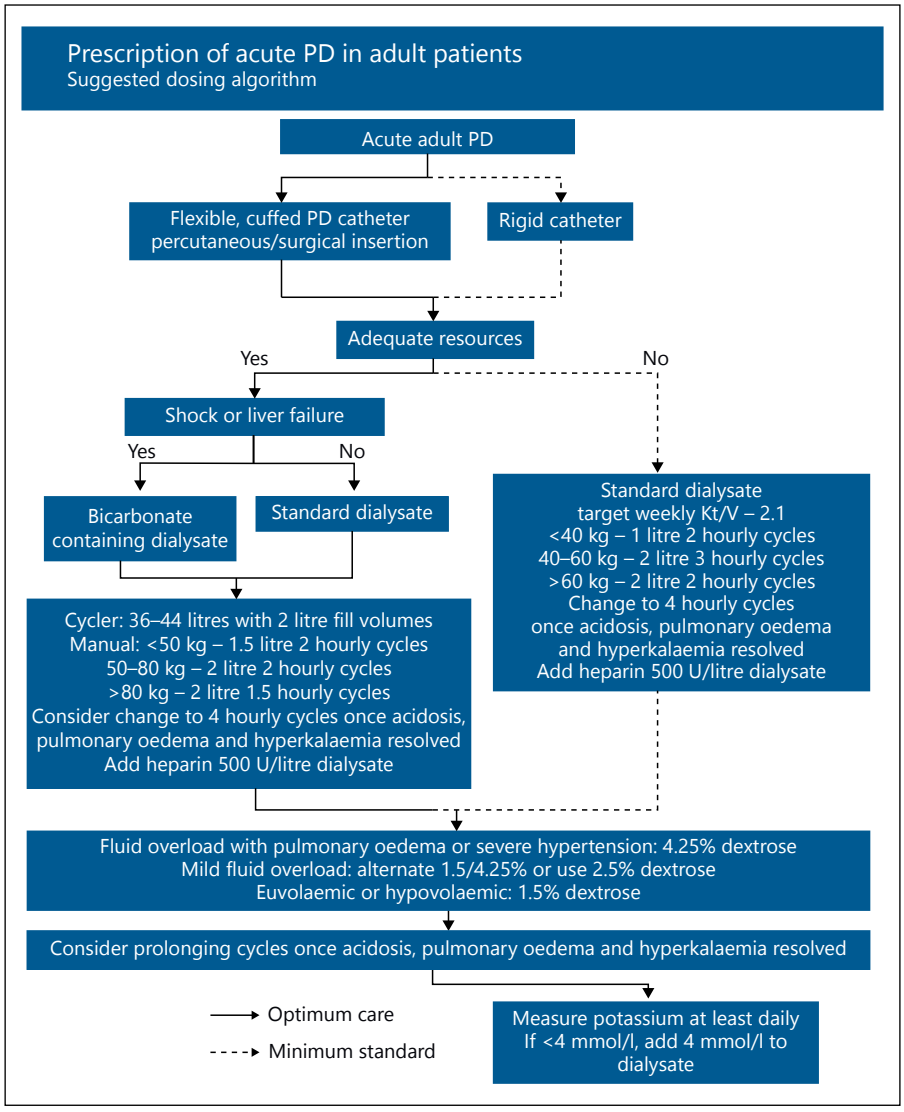

Fig. 1. Acute PD dosing guidelines adapted from ISPD guidelines [4].

CVVH (not published). They used tidal PD with biocompatible solutions, which differ from those of the Brazilian studies. The primary end point of 28-day survival was significantly higher in the PD group (69.8 vs. 46.8%, $p < 0.01$).

A systematic review published by Chionh et al. [22] concluded that there is no evidence to suggest significant differences in mortality between PD and extracorporeal blood purification in AKI and there is a need for good-quality evidence in this important area.

Recently, the Brazilian group published the largest cohort study of PD in AKI providing patient characteristics, clinical practice methods, patterns and their relationship to outcomes in a developing country [23]. Its objective was to describe the main determinants of patient and technique survival, including trends over time of PD treatment in AKI patients.

For comparison purposes, patients were divided into 2 groups according to the period of treatment: 2004–2008 and 2009–2014. A total of 301 patients were included, and 51 were transferred to HD (16.9%) during the study period. The main cause of technique failure (TF) was mechanical complication (47%) followed by peritonitis (41.2%). The risk of developing TF fell in the second period (RR 0.86, 95% CI 0.77–0.96) and three independent risk factors were identified: period of treatment at 2004 and 2009, sepsis and age >65. There were 180 deaths (59.8%) during the study period.

Patient survival improved between the 2 treatment periods with a RR reduction of 0.87 (95% CI 0.79–0.98). The independent risk factors for mortality were sepsis, age >70 and positive fluid balance. Finally, they observed an improvement in patient survival and TF rates along the years even after correction for several confounders.

Controversies

PD is relatively contraindicated in patients with recent abdominal surgery, adynamic ileus, intra-abdominal adhesions, peritoneal fibrosis, or peritonitis. However, in many countries with poor resources where there was no alternative treatment plan, PD may still be a lifesaving option in these patients albeit at higher risk.

Since volume and solute removal are slow and unpredictable parameters, PD may not be as efficient as extracorporeal blood purification techniques for the treatment of emergencies such as acute pulmonary edema or life-threatening hyperkalemia [4–6].

Another possible limitation of PD in AKI is that it is associated with protein losses and this may lead to extensive malnutrition. Protein losses as high as 48 g/day have been reported; however, many reports document the maintenance of serum albumin levels [24–26]. Protein supplementation, either enteral or parenteral (1.5 g/kg/day), has been recommended for AKI patients on PD [27].

The high glucose concentrations in peritoneal dialysate may cause hyperglycemia, even in non-diabetic patients. This is easily correctable through intravenous or intraperitoneal administration of insulin [26–28].

Góes et al. [29] performed an interesting prospective cohort study, and evaluated 208 sessions of HVPD in 31 AKI patients, aiming to evaluate metabolic implications and to identify risk factors associated with those metabolic effects. The glucose absorption remained at approximately 35.3 ± 10.5% per session, the protein loss measured 4.2 ± 6.1 g daily, with higher values initially, which declined significantly after 2 sessions, and the NB was initially negative, but stabilized at approximately zero after 3 sessions. The authors concluded that HPD did not increase hypercatabolism in AKI patients, and protein loss and glucose uptake remained constant during treatment. Those parameters were influenced by the clinical condition of the patients, including the cause of AKI, inflammation, and comorbidities – factors that should be known before the prescription of dialysis and nutrition, thus avoiding metabolic complications such as hyperglycemia, and worsening catabolism.

Peritonitis occurring in patients with AKI using PD as a modality of RRT can lead to very poor outcomes, and previous studies reported a frequency as high as 40% [6, 7, 24]. With better catheter-implantation techniques and automated methods, the incidence of peritonitis was reduced and the risk of causing infection in PD is similar to the risk with other forms of extracorporeal blood purification for AKI [6, 20, 23]. The most recent studies reported peritonitis levels from 12 to 15% and fungi and Pseudomonas aeruginosa were the most common agents responsible for transmitting the infection [6, 20, 23].

A previous study described that PD can increase intra-abdominal pressure (IAP) leading to impaired diaphragm mobilization, decreasing pulmonary compliance and ventilation, which may cause or worsen respiratory failure [30, 31]. However, PD is seldom the cause of ventilatory impairment in patients without pulmonary disease [30]. Almeida et al performed a prospective cohort study that evaluated respiratory mechanics during 44 HVPD sessions in 20 AKI patients undergoing mechanical ventilation and aimed to evaluate the respiratory mechanics, oxygenation and IAP. Their results showed increases in the pulmonary compliance without changes in respiratory system resistance. IAP increased significantly after the first dialysate infusion; however, after subsequent drainages these values decreased, reaching values close to baseline after the third PD session. Regarding oxygenation parameters, FiO2 did not change during the first and the second PD sessions and decreased after 2 sessions. PaO2/FiO2 increased progressively after a single dialysis session. The authors concluded that PD does not appear to worsen respiratory mechanics in AKI patients in spite of a modest increase in IAP [32].

Conclusion

This review clearly shows that PD is a simple, safe, and efficient way to correct metabolic, electrolyte, acid – base, and volume disturbances generated by AKI and it can be used as an RRT modality to treat AKI, both in and out of the ICU setting. The concerns regarding inefficiency were comparable with those of other modalities, and peritonitis, protein loss and respiratory mechanics have been largely dispelled. Recent reports have shown that in units regularly performing PD for AKI, mortality and complication rates have fallen further and there is no reason to believe that other modalities offer any outcome benefit

over PD. It is yet to be proven whether the more rapid recovery of renal function seen with acute PD has a long-term overall benefit compared to other modalities. The ISPD have firmly recommended that PD is a suitable modality for treating patients with AKI.

Disclosure Statement

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